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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/729,644	PIERCE ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,16-25,27-38,44-48,53,68,71 and 103-105* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,16-25,27-38,44-48,53,68,71 and 103-105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 April 2004 has been entered.

Claims 1-71 and 98-104 were pending and under consideration in the Final Office Action mailed 26 August 2003. Claims 3-15, 26, 39-43, 49-55, 57-67, 69-70 and 98-102 were canceled, claims 1, 2, 23, 24, 27, 29, 30, 32, 34, 38, 44, 46, 48, 56, 68, 71, and 103 were amended and claim 105 was added in the 27 April Paper. Claims 1, 2, 16-25, 27-38, 44-48, 53, 68, 71 and 103-105 are pending and under consideration.

Response to Amendment

Rejection of claims 3-15, 26, 39-43, 49-55, 57-67, 69-70 and 98-102 is moot in view of cancellation of the claims.

Claim Rejections - 35 USC § 112

Claims 1, 2, 16-25, 27-38, 44-48, 53, 68, 71 and 103-105 stand rejected under 35 U.S.C. 112, first paragraph, as lacking an enabling disclosure for reasons of record and herein below in the response to arguments.

Claim Rejections - 35 USC § 102

Claims 1, 2, 16, 23-25, 103 and 104 stand rejected and claims 68 and 105 are newly rejected under 35 U.S.C. 102(b) as anticipated by The Regents of the University of Michigan (WO 95/22611; hereinafter '611) for reasons of record and herein below in the response to arguments.

Claims 1, 2, 16, 23-25, 103 and 104 stand rejected and claims 27, 29-32, 34-37, 68 and 105 are newly rejected under 35 U.S.C. 102(e) as anticipated by Goldstein *et al.* (1996) U.S. Patent No. 5,962,427 (hereinafter Goldstein *et al.*) for reasons of record and herein below in the response to arguments.

Additional new grounds for objection and rejection are set forth herein below.

Response to Arguments

Comments re: Advisory Action

Applicant states, "the Examiner indicated that claim 1, as amended, recited a biocompatible matrix, rather than a biological matrix, as previously recited in claims 51 and 63" and urges, "previous amended claim 1, which recited biocompatible matrix, would encompass biological matrixes, and, therefore, does not constitute subject matter not previously considered by the Examiner" (Remarks, page 9). Applicant has mischaracterized the scope of the proposed amendment and the Examiner's position. The proposed amendment to claim 1 filed after final rejection read, "An in situ bioreactor, comprising a first nucleic acid molecule encoding a cell

growth stimulating agent, a second nucleic acid molecule encoding a bioactive agent, and a biocompatible substance capable of cellular infiltration, wherein the biocompatible substance is selected from the group consisting of: a polysaccharide, a PVA sponge, and a lactic acid/glycolic acid polymer" (emphasis added). The Examiner's position, as stated in the Advisory Action is, "[a]lthough 'polysaccharides' were previously set forth in claim 51 and a copolymer comprising lactic acid and glycolic acid was set forth in claim 63, claims 51 and 63 were limited to a biological matrix comprising a polysaccharide or copolymer comprising lactic acid and glycolic acid. In contrast, claim 1 is merely directed to a 'biocompatible substance' comprising a polysaccharide or a lactic acid/glycolic acid polymer" (emphasis added). Thus, the Examiner's position is not that a biocompatible matrix would not encompass a biological matrix, but that the biocompatible substances were not limited to being a matrix at all, and, therefore, the scope of the polysaccharide and lactic acid/glycolic acid polymer of the claims was broader than that of the previously examined claims.

Claim Rejections - 35 USC § 112

Claims 1, 2, 16-25, 27-38, 44-48, 53, 68, 71 and 103-105were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to use the claimed invention.

In response to the *prima facie* finding and arguments of record, Applicant again argues that the claimed invention is clearly distinguishable from replacement therapy methods wherein an endogenous gene is replaced with an exogenous nucleic acid in a cellular genome. Applicant alleges that gene therapy methods involving transgene expression are widely known and

established in the art. This argument has been fully considered but is not deemed persuasive. The basis of the enablement rejection is not the unpredictability of obtaining gene replacement by homologous recombination. Instead, the claims are not enabled in view of the broad and divergent scope of the claimed subject matter (*i.e.*, directed to therapeutic compositions comprising widely divergent active ingredients), the unpredictability of obtaining expression of sufficient level and duration to provide a therapeutic effect with any given potentially therapeutic nucleic acid, the underdeveloped state of the art relevant to the therapeutic use of the vast majority of embodiments of the invention recited in the claims and the absence of working examples. With regard to the alleged well-established nature of gene therapy methods involving transgene expression, Applicant cited numerous articles in response to the *prima facie* case which to support this position; however, each of these articles were considered and found to lack sufficient guidance to enable the instant claims for reasons set forth in the 26 August Office Action.

Next, Applicant again takes issue with the Examiner's contention that expression levels sufficient for systemic delivery of a bioactive agent would necessarily be of much greater magnitude and duration than those required for localized expression, as described in Roth *et al.* This argument was addressed in the Advisory Action mailed 22 March 2004. To summarize, the cited remarks were directed specifically to treatment of non-small cell lung cancer's using p53 as a bioactive agent as taught by Roth *et al.* Applicant had cited Roth *et al.* as evidence of enablement forth the instant claims. The Examiner's contention is merely that the teachings of Roth *et al.*, which are limited to treating non-small cell lung cancers by direct injection of a retroviral vector expressing a wild-type p53 gene, are not enabling for the instant claims because

the claims are explicitly limited to systemic delivery of the bioactive agent. It is highly unpredictable whether one could effectively treat non-small cell lung cancer by systemic administration of p53. Furthermore, as the teachings of Roth *et al.* are specifically directed to treating non-small cell lung cancers by direct injection of a retroviral vector expressing a wild-type p53 gene it is unclear how these teachings could be enabling for the broad scope of the instant claims.

With regard to the broader scope of the claims, Applicants submit that the skilled artisan would appreciate that the desired amount of systemically available bioactive agent will vary depending upon the agent itself, as well as any modifications that have been introduced. For example, where an agent has been modified to target a specific cell, less systemic agent is required in order to introduce sufficient amounts of the agent to the cell. Also, the skilled artisan would appreciate that expression levels may be modulated though the use of different promoters, which drive expression at different levels. However, this appears to be an invitation to the skilled artisan to experiment and discover for himself how to make each embodiment of the claimed invention such that it can be used therapeutically. Applicant argues that this experimentation would be merely routine; however, this position completely ignores the troubled history of the gene therapy art.

The claims are directed to a bioreactor which might comprise nucleic acids encoding any of dozens of biologically active proteins and teaches that the bioreactor is useful as a therapeutic, but fails to teach the skilled artisan how to obtain a therapeutic effect from any, let alone all of the embodiments recited in the claims. Applicant has taught the skilled artisan how to deliver a nucleic acid into a cell such that a heterologous protein is expressed therein and alleges that

developing each of the claimed bioreactors such that they can be used therapeutically is merely a matter of routine experimentation. As stated in the Final Office Action, "Applicant seems to be arguing that because the specification teaches how gene transfer can be achieved *in vivo*, which Crystal teaches was routine in 1995, using the claimed invention for the stated purpose of gene therapy would require only that the skilled artisan optimize the invention. However, the magnitude of experimentation required to 'optimize' the claimed invention is clearly illustrated by the fact that five years after Crystal declared gene transfer to be routine, Kay *et al.* teaches 'no clear-cut evidence of success with *in vivo* gene therapy'" (bridging pages 11-12).

Applicant reiterates arguments addressed in the 22 March Advisory Action based on *In re Wands* and *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.* which, while apparently acknowledging that experimentation would be required to practice the full scope of the invention, urge that the amount of experimentation is not undue according to the legal standard. As stated in the Advisory Action, "[t]hese arguments have been fully considered but are not deemed persuasive. With regard to the legal standard for 'undue experimentation', *In re Wands* is clear, 'Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* ...They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims' (8 USPQ2d 1400, page 1404)." Applicant's position appears to be an opinion of what is routine experimentation and not the legal analysis set forth in *In re Wands*. In contrast, analysis of the instant claims according to the "Wands factors" is

clearly set forth in the Office Action mailed 6 December 2002, and the arguments and evidence provided by Applicant to rebut the *prima facie* case has been found unpersuasive for reasons of record.

Finally, Applicant reiterates the argument based on *In re Brana* that enablement of the claimed invention does not require a demonstration that the invention may be used therapeutically because the Court held that the FDA's requirements of testing for safety and effectiveness are not required by the patent laws. As pointed out in the Advisory Action, the *Brana* court, citing *In re Krimmel*, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961), states, "proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility" (page 1442). The claims at issue in *In re Brana* were directed to a specific chemical compound having established antitumor activity, which was demonstrated in a recognized experimental animal model. In contrast, the instant claims are directed to an in situ bioreactor comprising active ingredients having broadly divergent properties, and the disclosure provides no evidence that the claimed invention can be used as asserted in the specification despite the established unpredictability of the art. Clearly, the courts finding in *In re Brana* does not support enablement for the instant claims.

Applicant's arguments have been fully considered but are not deemed persuasive individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement.

Claim Rejections - 35 USC § 102

Claims 1, 2, 23-25, 103 and 104 stand rejected and claims 68 and 105 are newly rejected under 35 U.S.C. 102(b) as anticipated by The Regents of the University of Michigan (WO 95/22611; hereinafter '611).

As described in the Office Action mailed 6 December 2002, the '611 application discloses a variety of growth stimulating agents, bioactive agents and biocompatible substances capable of cellular infiltration, and teaches combining the biocompatible substances capable of cellular infiltration with nucleic acids encoding the growth stimulating agents and/or bioactive agents and the implantation of the coated biocompatible substances capable of cellular infiltration into an animal (see throughout, especially the second full paragraph on page 7). In the paragraph bridging pages 18 and 19, the '611 application further teaches that the nucleic acids encoding growth stimulating agents and/or bioactive agents can be combined in a single application; thus, '611 teaches the "Bi-gene" device and *in situ* bioreactor of the instant application. . The '611 application also teaches the use of cell retention agents such as collagen and adhesive polypeptides, and genes encoding cell retention agents such as chemotactic agents (see especially the second full paragraph on page 13). Beginning at the final paragraph on page 31 and continued through the final paragraph on page 33, the '611 application teaches kits based on the disclosed devices.

Applicant has amended the claims such that they are now limited to comprising a specifically named "biological matrix", "cell growth stimulating agent" or "bioactive agent". Applicant argues that the art of record does not teach all of the elements of the amended claims. However, upon careful consideration of the cited art it is apparent that many embodiments of the

claimed invention are anticipated thereby. On page 25, lines 32-33, and page 27, lines 21-22, the '611 application contemplates a biological matrix that is a lactic acid/glycolic acid block copolymer according to claims 1 and 68. On page 13, line 34, the '611 application contemplates the growth stimulating agent FGF and in the second full paragraph on page 17, mutants thereof. Further, in the paragraph bridging pages 13-14, the '611 application contemplates the growth stimulating agents IGF and CSF. Thus, the bioreactor disclosed in the '611 application anticipates claim 2, 23-25 and 103-105.

Thus, for reasons of record, and herein above, claims 1, 2, 23-25, 68 and 103 and 104-105 are rejected under 35 U.S.C. §102(b) as anticipated by the bioreactor disclosed in the '611 application.

Claims 1, 2, 23-25, 103 and 104 stand rejected and claims 27, 29-32, 34-38, 68 and 105 are newly rejected under 35 U.S.C. 102(e) as anticipated by Goldstein *et al.* (1996) U.S. Patent No. 5,962,427 (hereinafter Goldstein *et al.*).

As described in the Office Action mailed 6 December 2002, Goldstein *et al.* discloses a variety of growth stimulating agents, bioactive agents and biocompatible substances capable of cellular infiltration, and teaches combining the biocompatible substances capable of cellular infiltration with nucleic acids encoding the growth stimulating agents and/or bioactive agents and the implantation of the coated biocompatible substances capable of cellular infiltration into an animal (see throughout, especially the fourth full paragraph in column 4). In the second full paragraph of column 17, Goldstein *et al.* further teaches that the nucleic acids encoding growth stimulating agents and/or bioactive agents can be combined in a single application; thus,

Goldstein *et al.* teaches the "Bi-gene" device and *in situ* bioreactor of the instant application. Goldstein *et al.* also teaches the use of cell retention agents such as collagen and adhesive polypeptides, and genes encoding cell retention agents such as chemotactic agents (see especially the fourth paragraph in column 10). Finally, in the first paragraph in column 11, Goldstein *et al.* teaches kits based on the disclosed devices.

Applicant argues that the art of record does not teach all of the elements of the presently amended claims (*Id.*). However, upon careful consideration of the cited art it is apparent that many embodiments of the claimed invention are anticipated thereby. In column 12, lines 46-49, Goldstein *et al.* contemplates a biological matrix that is a lactic acid/glycolic acid block copolymer according to claims 1 and 68. In column 14, line 26, Goldstein *et al.* contemplates the growth stimulating agent FGF and in the paragraph bridging columns 14-15, mutants thereof, which anticipates the mutant FGF of claims 2, 23-25 and 103-105. Further, in the second full paragraph in column 14, Goldstein *et al.* contemplates the growth stimulating agents IGF, VEGF and CSF according to claims 2, 23-25 and 103-105; the bioactive agents growth hormone and activin according to claim 27; factor VIII, factor IX, EPO, growth hormone, interleukin and interferon according to claims 29 and 34-37; the fibrinolytic anticoagulant tPA according to claims 30-32; and EPO according to claim 38.

Thus, for reasons of record, and herein above, claims 1, 2, 23-25, 27, 29-32, 34-38, 68 and 103-105 are rejected under 35 U.S.C. §102(e) as anticipated by the bioreactor disclosed by Goldstein *et al.*

New Grounds

Claim Objections

Claim 1 is objected to because of the following informalities: The claim recites the abbreviation PVA without providing a definition. Each abbreviation set forth in the claims should be accompanied by a definition the first time it is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 16-25 and 103-105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims are directed to a bioreactor comprising a mutated FGF having the properties of a "growth stimulating agent" as the term is defined in the first full paragraph on page 8 of the specification. The claim thus encompasses a genus of bioreactors comprising any and all mutated FGF molecules having the ability to promote cellular ingrowth/migration, survival/cellular maintenance, and/or proliferation either directly or indirectly. The Written Description Guidelines state "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436). The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). In the first paragraph on page 28, applicant provides two examples of a mutant FGF-2 that has the activity of a growth-stimulating agent (i.e. C78S and C96S) and cites prior art wherein these species were reduced to practice. Given that the claims encompass bioreactors comprising mutations at each and every amino acid in any FGF sequence, these two species are far from representative of the entire genus.

With regard to identifying characteristics, the Final Written Description Guidelines state that identifying characteristics include, "structure or other physical and/or chemical properties,...functional characteristics coupled with a known or disclosed correlation between function and structure or... a combination of such identifying characteristics..." (Federal Register, Vol. 66, No. 4, page 1106, column 3, second full paragraph). In order to fully describe

the structure of a polypeptide, Applicant must describe more than simply the primary amino acid sequence, as the functionality of a polypeptide is comprised within its higher order structure (i.e. secondary and tertiary structure). Because it is presently impossible to envision the higher order structure of a polypeptide based on a description of its primary structure alone, the skilled artisan would not recognize that Applicant was in possession of the genus of any mutant FGF polypeptides having the function of a growth stimulating agent based on a description of the primary structure of any mutant FGF polypeptide. As indicated in the Guidelines cited herein above, a genus of polypeptides might also be adequately described by disclosure of structural characteristics coupled with correlation of those structural characteristics with functional properties of the polypeptide. In the instant case, the disclosure provides that FGF-2 polypeptides wherein either one of two identified cysteine residues are substituted with serine residues retain the function of a growth stimulating agent. There is nothing in the disclosure, however, that would allow the skilled artisan to extend this knowledge beyond the disclosed species.

An adequate written description of a polypeptide requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polypeptide itself. It is not sufficient to define polypeptide solely by its principal biological property, i.e. it is a growth stimulating agent, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any polypeptide with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all polypeptide's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before

it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of bioreactors comprising all mutated FGF molecules having the ability to promote cellular ingrowth/migration, survival/cellular maintenance, and/or proliferation either directly or indirectly. Therefore, only the described bioreactor comprising a mutant FGF-2 wherein one or more cysteine residues is substituted by a serine residue meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

This rejection was originally set forth against claim 10, which was directed to a mutant FGF-2, and withdrawn when the claim was amended in the Paper filed 4 June 2003 such that the mutated FGF-2 was limited to one or more cysteine residues substituted by a serine residue. However, the mutant FGF of the present claims encompasses an even broader scope than the mutant FGF-2 of the originally filed claim 10.

In the Remarks that accompany the 4 June amendment, Applicant argues that the full scope of a mutant FGF-2 is fully described by the sequence of two mutant FGF-2 polypeptides having the identified characteristics and urges that description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species the genus embraces. Applicant's point is taken, as far as it goes.

However, The Guidelines for Written Description make clear, "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). Two species of FGF-2 are far from representative of a genus that embraces all mutant FGF's, wherein said mutant FGF's are of unlimited structure, having the properties of a growth stimulating agent.

Applicant further argues that the specification discloses sufficient identifying characteristics since it provides both a reference sequence and functional characteristics that may be used to identify a mutant FGF of the invention. This argument is not persuasive because the reference sequence is irrelevant in view of the fact that there is no limit on the degree to which the mutant protein can deviate from the reference sequence. Thus, the mutant FGF of the claims encompasses any protein having the recited function. As stated above, an adequate written description of a polypeptide requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polypeptide itself. It is not sufficient to define polypeptide solely by its principal biological property, i.e. it is a growth stimulating agent, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any polypeptide with that biological property.

The arguments of record in the Paper filed 4 June 2003 have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims are rejected under 35 U.S.C. §112, first paragraph, as lacking written description for a mutated FGF.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2 and 16 are rejected under 35 U.S.C. 102(e) as anticipated by Goldstein *et al.* (*supra*) as evidenced by Pidgeon *et al.* (2001) *Br. J. Cancer* 85:273-278.

Please note: Pidgeon *et al.* is not required for anticipation of the claims but is merely cited as evidence of properties that are inherent to the disclosure of Goldstein *et al.*

As described above, Goldstein *et al.* teaches all of the limitations of the *in situ* bioreactor of claim 2, wherein the cell growth-stimulating agent is a VEGF. Claim 16 is directed to the bioreactor of claim 2, wherein the cell growth-stimulating agent is an anti-apoptotic agent. Pidgeon *et al.* teaches that VEGF upregulates Bcl-2 and inhibits apoptosis in some cells (see throughout, especially Figures 1-3). Thus, the skilled artisan would understand that anti-apoptotic activity is inherent to the VEGF taught by Goldstein *et al.* and therefore the bioreactor of Goldstein *et al.* anticipates the limitations of claims 2 and 16.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

Anne-marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER